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Invited Editorial

Retrospective Exposure Assessment in Large Occupational Cohort Studies in China: Advantages and Concerns

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In epidemiological studies, accurate assessment of exposure to occupational and environmental risk factors is vital in investigating exposure–disease relationships. The basic principle of exposure assessment is to identify the variability of an agent within a given study population and to classify subjects accurately with respect to that variability. In the last fifteen years, there has been significant improvement in assessing occupational exposures (Stewart and Dosemeci, 1994). In the past, assessments were usually carried out by grouping subjects by occupation or industry, assuming that everyone in the same group was exposed at the same level; clearly not a reliable assumption. More recently, attempts have been made to reduce retrospective exposure misclassification, using plant/department/job title/calendar year combinations (Dosemeci *et al.*, 1990; Dosemeci and Stewart, 1996). This requires detailed historical information on the exposure of interest or its surrogates, such as organizational charts; plant layout; annual production or use of materials (with changes over time); use of chemicals and tools; hours per day, week or month of exposure; work activities and control measures; and periods of interruption due to layoffs or strikes. Accuracy of exposure assessment clearly depends on the availability of such information.

For the last fifteen years, I have been assessing occupational exposures in various large cohort and nested case-control studies; in particular, to benzene for 75,000 workers (Dosemeci *et al.*, 1994) and silica for 68,000 workers in China (Dosemeci *et al.*, 1993; Hayes *et al.*, 1997; McLaughlin *et al.*, 1992), and to phenol among 15,000 workers in five plants in the United States (Dosemeci *et al.*, 1991). In addition, I am currently assessing exposure to 45 different pesticides for 60,000 applicators in the United States, to diesel exhaust emission for 10,000 miners in 10 non-metal mines in the United States, and to various industrial chemicals for 75,000 women in a population-based cohort study in Shanghai.

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During these studies, I have found various advantages in China over Western countries. First, in China most of the historical exposure information needed is available in written records going back several decades. For example, we have over two million total dust measurements for the last forty years in our silica cohort. Other data are also available, such as annual production rates, detailed job descriptions and work activities, changes in production processes and control measures and, most importantly, subject-specific frequencies of exposure. In most epidemiologic studies, we seldom have subject-specific data and often assume that each worker was exposed for eight hours a day, five or six days a week, 22 or 26 days a month, and 11 or 12 months a year. It was surprising to learn from written records that the average exposure was only 4.2 hours per day in our benzene cohort study in China; an assumption of eight hours would have resulted in substantial inaccuracy.

A second advantage is the accessibility of this information. In the West, even when available, it is not always possible to access such written records, especially for earlier years due to various legal restrictions. Because almost all of the Chinese study sites are government-owned, once we had established collaboration with the Chinese Academy of Preventive Medicine, we had access to almost every door in all facilities and to all the relevant historical records. I remember, during my first visit to China in 1987, asking the plant manager whether we could see the so-called "Nutritional Records", which contain information on the subject-specific number of working days for each month. Before we had finished tea, a young local hygienist came to our guest-room with a large basket full of Nutritional Records hard-copied by year! I was astonished to see that the records went back to 1952, the first year of plant operation. I am not aware of anything comparable in a Western country.

An important advantage over the West is the homogeneity of exposures that workers tend to have, resulting from less complex exposure histories. For example, the average number of jobs per subject was 1.4 in our Chinese benzene cohort and 1.7 in the silica cohort, in contrast with 5–10 jobs in the United States (Stewart *et al.*, 1986). The lower number of jobs per subject produces more homogeneous exposure patterns.

Because of the large number of plants (for example, 700 factories in the benzene cohort and 29 mines and factories in the silica cohort), I could not visit every single site, and therefore depended on the local health professionals to provide reliable historical exposure information. Most of these were physicians trained in occupational health, including occupational hygiene and epidemiology, and I was impressed by their level of education and expertise. They were overseen by regional field supervisors, who were senior and experienced public health managers.

Another asset is the large number of subjects at high levels of exposure, compared with small numbers with even low-level exposures usually found in Western countries. This issue is particularly important if the association between exposure and outcome is weak. A large population with high levels of exposure can reveal a small but significantly increased risk which would not be detectable in small populations with low exposure.

When trying to estimate risk, confounding factors are almost as important as the main exposure itself. In our Chinese cohort studies, we were able to obtain the information necessary to assess exposure to potential confounders, such as radon, arsenic, nickel, polycyclic aromatic hydrocarbons in the silica study, and xylene and toluene in the benzene study. For example, we observed the great impact of these factors on the complex association between silica, silicosis and lung cancer (Cocco *et al.*, 1999).

There are, however, some concerns about the relevance of risk estimates obtained at very high exposure levels. For example, Abelson (1994) questioned the validity of linear extrapolation of risk from high to lower doses, arguing that at low exposure levels, risk might be overestimated if there is a threshold level in the dose–response relationship. However, as Portier *et al.* (1994) pointed out, linear extrapolation from high to low doses might actually underestimate risk in some circumstances. Indeed, Rappaport (1993) showed that metabolic saturations exist for some chemicals, and calculated that distortion from linearity for benzene, tetrachloroethylene and trichloroethylene starts at levels of 63, 22 and 178 mg/m^3, respectively, indicating that the risks of solvent-related outcomes do not necessarily rise linearly with increasing dose above the saturation point. Because of metabolic saturation at high levels of exposure, the actual risk at such exposures would be below the dose–response line, and linear extrapolation of risk from high to low doses could underestimate the risk at low levels. In any event, in our Chinese cohort studies, although average levels of exposure were higher than those observed now in Western countries, we still had sufficient subjects in low exposure categories to calculate risk at relatively low levels directly rather than by extrapolation. Other concerns relate to the comparability of sampling and analytical techniques in China and the West. Although there were some differences, variability within the same country has always been an issue, even in the West (Rice *et al.*, 1984).

All in all, there seems little doubt that the high quality historical data available in China results in substantially less exposure misclassification in large occupational cohort studies, with enormous advantages against relatively few concerns.

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